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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/806,400	03/30/2001	Yehuda Shoenfeld	01/21885	1174

7590 06/18/2002

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EXAMINER
SCHWADRON, RONALD B

ART UNIT	PAPER NUMBER
1644	//

DATE MAILED: 06/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/806,400	Shoenfeld et al.
Examiner	**Art Unit**
Ron Schwadron, Ph.D.	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Apr 23, 2002* .

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above, claim(s) *2-4, 8-11, 15-17, and 21-24* is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 5-7, 12-14, 18-20, 25, and 26* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☒ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

1. Claims 1,5-7,12-14,18-20,25,26 are under consideration.

RESPONSE TO APPLICANTS ARGUMENTS

2. The first line of the specification should be amended to indicate that the instant application is a national stage filing under 35 U.S.C. 371 of PCT/IL99/00519 .

3. The amendment filed 4/23/2002 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows. There is no support in the specification as originally filed for the recitation of "the composition being formulated for inducing oral tolerance" in the abstract filed with the amendment filed 4/23/2002. Regarding applicants comments about the specification, pages 15 and 16, said pages disclose a specific method for preparing oxidized LD, they do not disclose "the composition being formulated for inducing oral tolerance". The specification and original claims disclose that the claimed invention contained oxidized LDL and a pharmaceutically acceptable carrier. The specification does not disclose that oxidized LDL requires any particular manipulation or formulation to render it tolerogenic. The limitation "the composition being formulated for inducing oral tolerance" would seem to encompass further processing of the oxidized LDL component. However, there is no disclosure in the specification as originally filed of the scope of the claimed invention which encompasses oxidized LDL being formulated for inducing oral tolerance. There is no written description of the scope of the claimed invention in the specification as originally filed (eg. the claimed invention constitutes new matter).

Applicant is required to cancel the new matter in the reply to this Office Action.

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1,5-7,12-14,18-20,25,26 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention for the reasons elaborated in the previous Office Action. Applicants arguments have been considered and deemed not persuasive.

Claim 1 is indefinite in the recitation of "modified LDL" because it is unclear what this term means or encompasses. It has no art recognized meaning and the meaning of said term is not disclosed in the specification.

Regarding applicants comments about US Patent 5,407,710, said patent is called "Laser interconnection of circuits on transplant substrate", the inventors are Baum et al., and the term "modified LDL" is not disclosed in said patent. Regarding applicants comments about several other references disclosed in page 3 of the instant amendment, third paragraph, the references cited were not of record and copies were not supplied so said references were not considered.

Claims 7 and 20 are indefinite in that "active derivative" lacks antecedent basis in claim 1 or 14 respectively.

Regarding applicants comments, claims 1 and 14 recited "active component selected from the group consisting of" wherein "active derivative" is not a member of the Markush group recited in said claims. Therefore "active derivative" lacks antecedent basis in claim 1 or 14 respectively.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1,5-7,12-14,18-20,25,26 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

There is no support in the specification as originally filed for the recitation of "the composition being formulated for inducing oral tolerance" in claim 1. Regarding applicants comments about the specification, pages 15 and 16, said pages disclose a specific method for preparing oxidized LD, they do not disclose "the composition being formulated for inducing oral

tolerance". The specification and original claims disclose that the claimed invention contained oxidized LDL and a pharmaceutically acceptable carrier. The specification does not disclose that oxidized LDL requires any particular manipulation or formulation to render it tolerogenic. The limitation "the composition being formulated for inducing oral tolerance" would seem to encompass further processing of the oxidized LDL component. However, there is no disclosure in the specification as originally filed of the scope of the claimed invention which encompasses oxidized LDL being formulated for inducing oral tolerance. There is no written description of the scope of the claimed invention in the specification as originally filed (eg. the claimed invention constitutes new matter).

There is no support in the specification as originally filed for the recitation of "thereby inhibiting at least one atherosclerosis-related symptom in said subject" in claim 14. This limitation is not disclosed in the specification or claims as originally filed. There is no written description of the scope of the claimed invention in the specification as originally filed (eg. the claimed invention constitutes new matter).

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> > (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
> >
> > (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

9. Claims 1,5,7,12,14,18,20,25 stand rejected under 35 U.S.C. 102(b) as being anticipated by Yesair et al. (US Patent 4,874,7695) for the reasons elaborated in the previous Office Action. Applicants arguments have been considered and deemed not persuasive.

Yesair et al. teach a composition for oral administration containing LPC (see column 5, last paragraph and Examples). The recitation of an intended use carries no patentable weight in the instant product claims (eg. 1,5,7,12). LPC is a derivative of LDL (see claim 12). LPC is also

a derivative of Ox LDL (see specification, page 5, first complete paragraph). LPC is a modified LDL. The pharmaceutically acceptable carrier is the other lipids contained in the composition taught by Yesair et al. (see column 5). Yesair et al. teach the in vivo administration of said composition (see Examples and column 13, last paragraph). It is an inherent property that administration of the claimed composition results in the method of claim 14, because the method taught by Yesair et al. involves administration of the same compound (LPC) to the same population (eg. any individual, because it would be desirable to prevent atherosclerosis in any individual).

Regarding applicants comments, the Shen et al. and Maurer et al. references were not of record and copies were not submitted, so said references were not considered and applicants comments regarding said references were not considered. Regarding applicants comments about pages 15 and 16 of the specification, there is no evidence of record that the method used to prepare oxidized LDL is anything other than the art recognized method to prepare oxidized LDL. Regarding applicants comments about oral tolerance and the compound taught by Yesair et al., the MPEP section 716.01(c), page 700-217 (August 2001) states:

ATTORNEY ARGUMENTS CANNOT TAKE THE PLACE OF EVIDENCE

The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant.

There is no evidence of record that the composition taught by Yesair would not induce oral tolerance. The specification discloses that Ox LDL can be used to induce oral tolerance. It does not disclose that Ox LDL has to be administered in any particular form to induce oral tolerance.

10. Claims 1,5-7,12,13 are rejected under 35 U.S.C. 102(e) as being anticipated by Witztum et al. (US Patent 6,225,070) for the reasons elaborated in the previous Office Action. Applicants arguments have been considered and deemed not persuasive.

Witztum et al. teach a composition containing MDA-LPL or oxidized LPL or Acetyl-LDL in PBS (see column 18). The recitation of an intended use carries no patentable weight in the instant product claims. The pharmaceutically acceptable carrier is PBS (see column 18, lines 55 and 56).

Regarding applicants comments, the Ogra et al. and Chen et al. references were not of record and copies were not submitted, so said references were not considered and applicants comments regarding said references were not considered. The recitation of an intended use carries no patentable weight in the instant product claims. There is no evidence of record that establishes that the Ox LDL taught by Witztum could not be used to induce tolerance. Regarding applicants comments about oral tolerance and the compound taught by Witztum et al., the MPEP section 716.01(c), page 700-217 (August 2001) states:

ATTORNEY ARGUMENTS CANNOT TAKE THE PLACE OF EVIDENCE

The arguments of counsel cannot take the place of evidence in the record. In re Schulze, 346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results, commercial success, solution of a long-felt need, inoperability of the prior art, invention before the date of the reference, and allegations that the author(s) of the prior art derived the disclosed subject matter from the applicant.

The specification discloses that Ox LDL can be used to induce oral tolerance. It does not disclose that Ox LDL has to be administered in any particular form to induce oral tolerance.

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. Claims 1,5-7,12,14,18-20,25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Strober et al. in view of Hansson et al., Resch et al. and Sima et al. for the reasons

elaborated in the previous Office Action. Applicants arguments have been considered and deemed not persuasive.

Strober et al. teach compositions of autoimmune antigens and the use of said compositions to treat autoimmune disease (see abstract). Strober et al. teach that the orally administered composition contains autoantigen and a pharmaceutically acceptable carrier (see page 7, last paragraph). Strober et al. teach that said method can be used to treat autoimmune disease mediated by T cells or B cells (see page 5). Strober et al. do not teach use of the antigens recited in the claims to treat atherosclerosis. Hansson et al. teach that Ox LDL functions as an autoantigen in atherosclerosis (see abstract). Sima et al. also teach that Ox LDL functions as an autoantigen in atherosclerosis (see sixth line from bottom). Sima et al. also teach that autoantibodies bind modified/derivatives of LDL (eg. glycated LDL or HNE-Lys). Resch et al. that autoantibodies bind modified/derivatives of LDL (eg. HNE-LDL or MDA-LDL). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Strober et al. teach compositions of autoimmune antigens and the use of said compositions to treat autoimmune disease while Sima et al., Resch et al. and Hansson et al. teach that modified LDL/Ox LDL are autoantigens involved in atherosclerosis. One of ordinary skill in the art would have been motivated to do the aforementioned because Strober et al. teach that said treatment can be used to treat "any other autoimmune disease now known or discovered in the future"(see page 5, lines 20,21).

Regarding applicants comments, Hansson et al. teach that Ox LDL functions as an autoantigen in atherosclerosis (see abstract), Sima et al. also teach that Ox LDL functions as an autoantigen in atherosclerosis (see sixth line from bottom), Sima et al. also teach that autoantibodies bind modified/derivatives of LDL (eg. glycated LDL or HNE-Lys) and ch et al. that autoantibodies bind modified/derivatives of LDL (eg. HNE-LDL or MDA-LDL). Hansson et al. disclose "This data emphasize the importance of inflammation and immune responses in the pathogenesis of atherosclerosis" (see last sentence of abstract). Regarding various references referred to by applicant that are not of record and of which copies were not supplied, said references and applicants comments regarding said references were not considered. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Strober et al. teach compositions of autoimmune antigens and the use of said compositions to treat autoimmune disease while Sima et al., Resch et

al. and Hansson et al. teach that modified LDL/Ox LDL are autoantigens involved in atherosclerosis. One of ordinary skill in the art would have been motivated to do the aforementioned because Strober et al. teach that said treatment can be used to treat "any other autoimmune disease now known or discovered in the future"(see page 5, lines 20,21).

13. No claim is allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 1600 at (703) 308-4242.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Monday through Thursday from 7:30 to 6:00. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group ~~180~~ 1600 receptionist whose telephone number is (703) 308-0196.

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644